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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/244,984	02/04/1999	ROY A. BLACK	16761/153	4402

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EXAMINER

MORAN, MARJORIE A

ART UNIT	PAPER NUMBER
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1631

DATE MAILED: 10/02/2002

23

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/244,984

Applicant(s)

BLACK ET AL.

Examiner

Marjorie A. Moran

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 09 July 2002.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 41,42,56-63 and 66-74 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 41,42,56-63 and 66-74 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 09 July 2002 is/are: a) ☐ accepted or b) ☒ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____
- 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____

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The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action. All objections and rejections not reiterated below are hereby withdrawn. Claims 41-42, 56-63, and 66-74 are pending.

Drawings

The corrected or substitute drawings were received on 7/9/02. The drawings are objected to by the draftsman as set forth on Form PTO 948.

Specification

The pages of the specification have been renumbered by the examiner in order to comply with 37 CFR 1.52 (b) (5), which requires that pages of the specification including claims and abstract must be numbered consecutively, starting with 1. The pages of the specification are now numbered 1-92. All of the changes are not enumerated herein; however for applicant's convenience, it is noted that the page containing the title "Summary of the Invention" is now page 3, the page wherein the "Brief Description of the Figures" begins is now page 10, the "Detailed Description of the Invention" now begins at page 12, Table 1 is listed on pages now numbered 41-78, the originally filed claim pages are now numbered 81-91, and the abstract page is now numbered page 92.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

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The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 41-42, 56-63, and 66-74 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a NEW MATTER rejection.

A step of using atomic coordinates comprising a "substantial part" of Table 1 wherein the "substantial part" comprises atomic coordinates comprising an S1' pocket, an S1'S3' pocket, or atoms which bind a catalytic zinc, is new matter.

Original claim 53 recited a TACE crystal with a unit cells comprising four independent catalytic domain molecules, but did not specifically identify "pockets" or zinc binding atoms. Original claims 56-57 limited an *associated compound* identified in the method to one which associates with an S1' region or an S1'S3' pocket, but did not limit the TACE itself to be represented by a "substantial portion" of a set atomic coordinates, wherein that portion defines an S1' or S1'S3' pocket. Original claim 58 limits an associated compound to incorporate a moiety which chelates zinc. The original claims did not limit the atomic coordinates of TACE to include any specific atoms which "bind a catalytic zinc". Pages 3 and 7 of the originally filed specification disclose a polypeptide characterized by the structural coordinates of Table 1 "or a substantial part" thereof, but do not define the "substantial part" anywhere. Similarly,

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page 32 discloses that a computer readable medium may comprise the coordinates of Table 1 or a "substantial portion thereof", but does not define the "substantial portion". Page 26 of the originally filed specification discloses a description of the entire TACE molecule, wherein the polypeptide comprises a number of regions, including those identified as S1' and S1'S3' pockets, and residues which bind a catalytic zinc are identified. However, as set forth above, the description on page 26 is for the entire molecule, and is not a teaching for a "substantial portion" of the coordinates of Table 1, nor is it a teaching that any particular portion of a TACE polypeptide should be "used" to design an associated compound. Pages 8 and 33 disclose particular limitations of a compound which associates with TACE, specifically that such compounds should be designed to associate with an S1' or S1'S3' pocket, or should incorporate a moiety which chelates zinc. It is noted that these are descriptions of an associated compound, NOT a description of TACE or a "substantial portion" of TACE. While the entirety of a TACE molecule would be expected to comprise an S1' pocket, an S1'S3' pocket, and zinc-binding residues, and therefore the entirety of Table 1 is expected to contain atomic coordinates which represent these regions, neither the originally filed specification or claims taught or recited a "substantial portion" (i.e. less than the entirety) of Table 1 which comprises coordinates representing an S1' pocket, an S1'S3' pocket, or atoms which bind a catalytic zinc. In the response filed 7/9/02, applicant does not point to support for the newly claimed limitations, and none is apparent, as set forth above, therefore the claims are rejected for reciting new matter.

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Claims 41-42 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. This is an ENABLEMENT rejection.

The factors to be considered in determining what constitutes undue experimentation were affirmed by the court in *In re Wands* (8 USPQ2d 1400 (CAFC 1986)). These factors are the quantity of experimentation; the amount of direction or guidance presented in the specification; the presence or absence of working examples; the nature of the invention; the state of the prior art; the level of skill of those in the art; predictability or unpredictability of the art; and the breadth of the claims.

Neither the prior art nor the specification teach how to identify an inhibitor, modulator or other regulator of TACE using only the method steps recited. The instant specification teaches on page 23 that the inventive methods may be used to identify potential inhibitory, mediatory, or regulatory compounds or compounds which have other binding effects, and discloses that one can evaluate the probability for synthesizing and testing inoperative compounds. It is well known in the art that not every compound which binds to an enzyme is an inhibitor. It is also well known a compound may bind to an enzyme without necessarily affecting its activity. For example, a compound which binds to a catalytic site may easily be an agonist instead of an antagonist. An antibody may bind to an epitope on an enzyme not involved in activity; or a compound may "associate" with the enzyme through very weak interactions and not affect activity at all. Water and/or salt molecules would be expected to associate with any polypeptide in solution, but do not necessarily inhibit, modulate, or regulate the activity of the polypeptide.

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Claim 63 merely recites steps identifying a compound which "associates with" TACE; no steps of actually identifying an associating compound as an inhibitor, modulator, or regulator is recited in the claims. The instant specification teaches on pages 79-80 (Example 5) a method wherein a known inhibitor of TACE was modeled and "fitted" to a TACE catalytic site using atomic coordinates for both TACE and the inhibitor, then "specific candidate inhibitor-TACE interactions" were determined and used to identify other putative inhibitors. No step of determining or using specific candidate inhibitor-TACE interactions are recited in the rejected claims. Although the level of skill in the art is acknowledged to be high, in the absence of a step to identify whether the associating compound of claims 63 is indeed an inhibitor, modulator, or other regulator of TACE, it would require undue experimentation for one skilled in the art to determine whether the identified compound is an inhibitor, modulator, or other regulator of TACE. For these reasons, claims 41 and 42 are not enabled.

Claim Rejections - 35 USC § 101

Claims 56-63 and 67-74 are rejected under 35 USC 101 because the claimed invention lacks patentable utility.

Applicant's arguments with respect to claims 56-63 have been considered but are moot in view of the new ground(s) of rejection. As applicant's arguments apply to utility, they are addressed herein.

In response to the argument that results which may be presented in tabular, graphical or sterical form are "concrete and tangible" results, it is noted that the claims

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do not recite any such output nor a step of generating a table or graph, etc. and (b) a step or limitation to produce a graph or table does not necessarily mean that the claims meet the requirements for utility. In the instant case, since the claims are directed to a method wherein all steps are performed on a computer (i.e. there is no "safe harbor"; e.g. a physical act performed outside the computer), the question is actually, as argued by applicant, whether the claimed method produces a concrete, tangible AND useful result. Applicant argues that the invention is useful for searching for compounds which interact with TACE. In response, it is noted that a method which identifies an inhibitor of TACE does provide a concrete, tangible and useful result, for the reasons set forth on page 2 of the instant specification. However, a method which only identifies a compound which interacts/associates with TACE does not provide a useful, concrete and tangible result, as the activity of the associating compound, and/or its effect on TACE, is completely unknown. A "use" to do further research does not meet the utility requirements under 35 USC 101. As further research would have to be performed to determine what, if any, activity or effect the identified compound would have, the result of the method is not a useful, concrete and tangible one. It is noted that mere "association" with a catalytic domain is not evidence that a compound is necessarily an inhibitor of the enzyme. See above. It is not known what effect a modulator or regulator other than an inhibitor would have on TACE, and thereby on $\text{TNF}\alpha$ production (i.e. it is not known whether a compound which upregulates TACE necessarily result in higher levels of $\text{TNF}\alpha$), therefore identification of a compound which merely modulates TACE

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production or activity is not a concrete, tangible, and useful result. For these reasons, the claimed subject matter does not have utility and the claims are rejected.

Conclusion

No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Marjorie A. Moran whose telephone number is (703) 305-2363. The examiner can normally be reached on Monday to Friday, 7:30 am to 4 pm EST.

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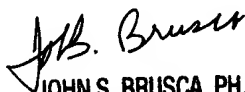
If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward can be reached on (703) 308-4028. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 for regular communications and (703) 872-9306 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to a patent analyst, Tina Plunkett, whose telephone number is (703) 305-3524.



Marjorie A. Moran
Examiner
Art Unit 1631

October 1, 2002



JOHN S. BRUSCA, PH.D
PRIMARY EXAMINER